



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/037,718	01/04/2002	Ralph Evan McGinnis	2DLSM&R12/01	7724

7590  
Robert McGinnis  
1575 West Kagy Blvd.  
Bozeman, MT 59715

EXAMINER
----------

WHALEY, PABLO S

ART UNIT	PAPER NUMBER
----------	--------------

1631

MAIL DATE	DELIVERY MODE
-----------	---------------

09/22/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/037,718	<b>Applicant(s)</b> MCGINNIS ET AL.	
	<b>Examiner</b> PABLO WHALEY	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 05 May 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 91-166 is/are pending in the application.
- 4a) Of the above claim(s) 140-166 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 91-139 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/19/2008</u> .   | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Claims Under Examination***

Claims 91-166 are pending. Claims 1-90 are cancelled. Claims 140-166 are again withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or species, there being no allowable generic or linking claim.

### ***Priority***

After further consideration, applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows: The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). The disclosure of the prior-filed application, Application No. 09/947,768, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. In particular, Application No. 09/947,768, fails to provide adequate support for claim 91, which requires oligonucleotides complimentary to a group of covering markers, wherein the group comprises thousands of bi-allelic markers with least common allele frequencies less than or equal to 0.3.

***Information Disclosure Statement***

The information disclosure statement filed 05/19/2008 has been considered in full.

***Withdrawn Rejections***

The rejection of claims 91-139 are rejected under 35 U.S.C. 112, second paragraph, in the Office action mailed 11/01/2007 is withdrawn in view of applicant's arguments and amendments to the claims, filed 05/05/2008.

The rejection of claims 91-139 under 35 U.S.C. 101 for non-statutory subject matter is withdrawn in view of applicant's arguments, filed 05/05/2008.

The rejection of claims 91-139 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cohen et al. in view Kruglyak et al. is withdrawn in view of applicant's arguments directed to the teachings of Kruglyak, filed 05/05/2008.

***Claim Rejections - 35 USC § 112, 2<sup>nd</sup> Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 91-139 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims that depend directly or indirectly from claim 91 are also rejected due to said dependence.

Art Unit: 1631

Claim 91 recites the limitation “being complementary to a group of two or more bi-allelic markers, ... , wherein the group of covering markers comprises thousands of bi-allelic markers.” A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). In the present instance, claim 91 recites the broad recitation “two or more”, and the claim also recites “thousands” which is the narrower statement of the range/limitation. This rejection is newly applied.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Art Unit: 1631

Claims 91-139 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cohen et al. (US 5,945,522; Issued Aug. 31, 1999; Filed Dec. 22, 1997), in view of Kruglyak et al. (Am. J. Hum. Genet., 1995, Vol. 57, p.439-454), in view of Cohen (EP 0892068; Date of Publication: 20 Jan 1999; IDS filed 05/20/2008).

This rejection is newly applied.

Cohen (1997) teaches a gene associated with prostate cancer in humans. In particular, the invention provides oligonucleotides which are used to detect the presence of bi-allelic sites that are in linkage disequilibrium with the PG1 gene for use in determining the risk of prostate cancer [Col. 6, lines 5-25]. Bi-allelic sites are systematically verified by comparing the sequences of both strands of each pool (i.e. enabling selection of complementary markers) [See Col. 16, Example 2]. Cohen (1997) shows lowest allele frequencies of bi-allelic polymorphisms below 1% (i.e. rare mutations) in the human genome and minor allele frequencies as low as 0.16 [Col. 52, Table 1]. Cohen (1997) teaches analysis for identifying polymorphisms in chromosomal regions [Col. 10], and haplotype analysis for estimating frequencies in a population and genetic mapping [Col. 13]. Cohen (1997) teaches major and minor allele frequencies are determined, wherein the frequency of bi-allelic polymorphisms detected is  $0.3 \pm 0.05$  for the minor allele [Col. 10, last ¶ and Col. 11, first ¶]. Cohen (1997) teaches methods are also provided for the selection of complementary sequences [Col. 5, lines 40-50]. Cohen (1997) teaches quantitative analysis of gene expression may also be performed using arrays, wherein the term array means a one dimensional, two dimensional, or multidimensional arrangement of a plurality of nucleic acids of sufficient length to permit specific detection of expression of mRNAs capable of hybridizing thereto [See Example 12]. Figures 2, 3, and 4 show linkage analysis results with sequencing results for determining the distance between markers.

Cohen (1997) does not teach markers chosen so that a CL-F region is systematically covered by the covering markers, as in claims 91-94. However, this is a functional limitation of the claimed bi-allelic covering markers, and not the claimed composition per se. The MPEP [Section 2112] states that where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, rejection under 35 USC 103 is proper when rationale is provided to show inherency. In the instant case, Cohen (1997) teaches oligonucleotides with minor allele frequency values less than 0.3 [Table 1], analysis for identifying polymorphisms in chromosomal regions [Col. 10], and haplotype analysis for estimating frequencies in a population and genetic mapping [Col. 13]. A review of the specification teaches that a CL-F region can be represented on CL-F map [p.14], wherein a CL-F map comprises CL-F points [p.13] representing a value for a chromosomal location coordinate and a least common allele frequency coordinate [p.12] for individual bi-allelic markers and genes. Cohen (1997) teaches probes that hybridize to polymorphisms (i.e. bi-allelic markers) possessing specific characteristics of minor allele frequency and chromosomal length (i.e. covering) at various locations in a chromosome. Therefore, Cohen (1997) inherently teaches oligonucleotides with characteristic properties for binding with bi-allelic markers chosen so that a CL-F region and CL-F map are systematically covered by said markers, as in claims 91-94.

Cohen (1997) does not teach least common allele frequency values less than or equal to 0.1, as in claims 96-103. However, it would have been obvious to investigate oligonucleotides that are complementary to rare polymorphism markers chosen to cover in CL-F maps and regions, as claimed, since Cohen (1997) shows lowest allele frequencies of bi-allelic polymorphisms below 1% (i.e. rare mutations) in the human genome and minor allele frequencies of 0.16 [Col. 52, Table 1]. One of ordinary skill in the art would have been motivated to include the rarest alleles (i.e. least allele frequencies less than 0.1) in order to create a more robust genotyping test by including with fewer false positive results.

Cohen (1997) does not teach a CL-F region being a collection of points in a two-dimensional CL-F map that is similar to an x-y graph, as in claims 91-94.

Cohen (1997) does not teach oligonucleotides that are complementary to thousands of bi-allelic markers, as in claim 91.

Kruglyak teaches the use of genetic markers in a multipoint analysis [Abstract]. In particular, Kruglyak teaches two-dimensional chromosomal genetic map of biallelic markers for multipoint analysis using dozens of markers that is similar to an x-y graph [Abstract, p.441, and Fig. 1]. Kruglyak teaches markers covering various chromosomal positions [Fig. 2]. The program requires pedigree information, genotype information, and a map file of location and frequencies of genetic markers [p.441, Col. 2, MAPMAKER]. Kruglyak does not specifically teach a CL-F map showing minor allele frequency versus chromosomal length. However, it would have been obvious to one of ordinary skill in the art to use graphs similar to an x-y graph for showing minor allele frequency versus chromosomal length in genotyping studies, since Kruglyak teaches two-dimensional graphs showing probability versus chromosomal length, allele sharing versus chromosomal position [Fig. 1, 2, and 3].

Cohen teaches (1999) teaches that there are more than one thousand bi-allelic markers for use in a high density bi-allelic marker map [p.5, Suggested Strategies, and p.10, Map Characteristics, and Example 10], as in claim 91.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to use the oligonucleotides taught by Cohen (1997) to cover chromosomal regions in a two-dimensional map (i.e. CL-F map) showing minor allele frequency versus chromosomal length, as suggested by Kruglyak, since Cohen (1997) teaches minor allele frequencies and since Kruglyak teaches a two-dimensional chromosomal map of biallelic markers [Abstract, p.441, Fig. 2]. One of ordinary skill in the art would have been motivated to use the oligonucleotides as set forth above in order to provide



Art Unit: 1631

visual analysis of markers spaced at various regions on a chromosome, as suggested by Kruglyak [Fig. 2].

It would further have been obvious to someone of ordinary skill in the art at the time of the instant invention to create a set of oligonucleotides as taught by Cohen (1997) that are complementary to thousand of biallelic markers, as taught by Cohen (1999), since Cohen (1997) teaches association studies showing thousands of bi-allelic markers [Col. 11, lines 1-20]. One of ordinary skill in the art would have been motivated to use more markers to improve to diagnostic power of the association and linkage analysis, as suggested by Cohen (1999) [p.17, Example 9 and 10].

Claims 91-139 are rejected under 35 U.S.C. 103(a) as being unpatentable over McGinnis et al. (WO/1999/43858; International Publication Date: 2 Sept 1999), in view of Cohen (EP 0892068; Date of Publication: 20 Jan 1999; IDS filed 05/20/2008).

This new grounds of rejections is necessitated by applicant's arguments, filed 05/05/2008, that Kruglyak does not teach CL-F maps and CL-F regions.

McGinnis teaches oligonucleotides complementary to markers within specific CL-F distances in a CL-F region of CL-F maps [p.9, p.14-16, p.31, p.35, Example 1S, p.36, and Ref. Claims 51-88]. McGinnis teaches two-dimensional linkage analysis methods wherein the set of markers systematically scan or "cover" a two-dimensional region having dimensions of chromosomal location and least common allele frequency, and bi-allelic markers having least common allele frequencies less than 0.3, 0.2 or even less than 0.1 have an important place in linkage [p.7, lines 19-39, and p.44, lines 23-33].

McGinnis does not teach oligonucleotides that are complementary to thousands of bi-allelic markers, as in claim 91.

Cohen teaches (1999) teaches that there are more than one thousand bi-allelic markers for use in a high density bi-allelic marker map [p.5, Suggested Strategies, and p.10, Map Characteristics, and Example 10], as in claim 91.

It would further have been obvious to someone of ordinary skill in the art at the time of the instant invention to create a set of oligonucleotides as taught by McGinnis that are complementary to thousand of biallelic markers, as taught by Cohen (1999), since Cohen (1999) teaches association studies using thousands of markers [p.17]. One of ordinary skill in the art would have been motivated to use more markers to improve to diagnostic power of the association and linkage analysis, as suggested by Cohen (1999) [p.17, Example 9 and 10].

### ***Response to Arguments***

Applicant's arguments, filed 5/5/2008, that the cited references render the claimed subject matter obvious in view of unexpected results have been fully considered but are not persuasive. In response, the MPEP Section 716.01(c) states that unexpected results must be established by factual evidence. Applicants have not presented any experimental data showing that the catalytically generated metallic precipitates on microarray technology results in an unexpected advantage. Applicant's reference to the specification [p.21] does not present any experimental data showing unexpected results. Due to the absence of experimental data, tests, or calculations comparing applicant's power studies using bi-allelic markers with lower minor allele frequencies with those of the closest prior art, applicant's assertion of unexpected results constitute mere argument. See also *In re Linder*, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972; *Ex parte George*, 21 USPQ2d 1058 (Bd. Pat. Appl. & Inter. 1991). Applicant is reminded that arguments should refer only to the specification as filed, and not to paragraphs numbers in the published application since the published application is not contained in the application file.

Art Unit: 1631

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached at 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

**/Pablo S. Whaley/**

Patent Examiner

Art Unit 1631

/John S. Brusca/

Primary Examiner, Art Unit 1631